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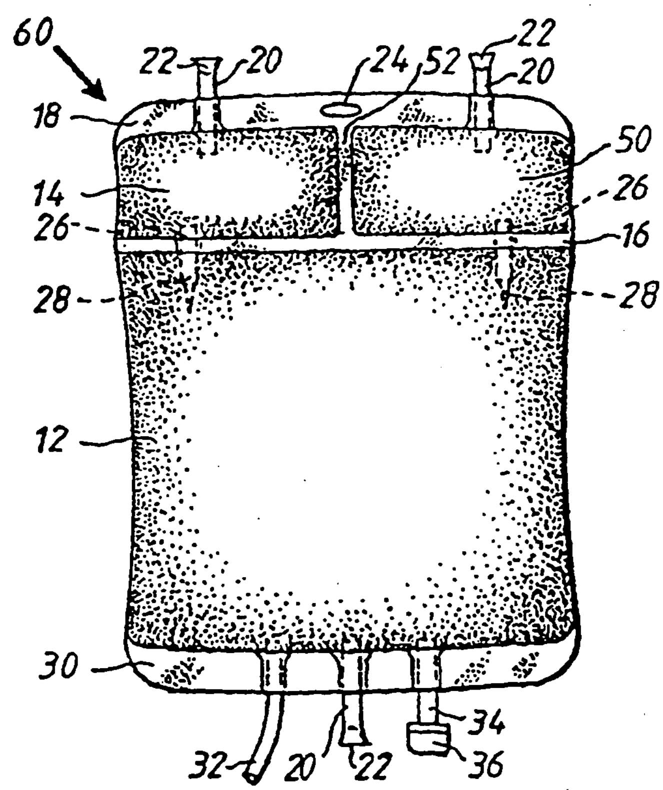
(54) Title: METHOD AND APPARATUS FOR REDUCING THE DEGRADATION OF HEAT SENSITIVE COMPONENTS IN MEDICAL SUBSTANCES DURING HEAT STERILISATION

(57) Abstract

A method and an apparatus (40) for reducing the degradation of heat sensitive components in medical substances during heat sterilisation are described. The medical substances are contained in a multiple chamber recipient (10, 60) that comprises a first chamber (12) with a first medical substance and at least one second chamber (14, 50) containing an amount of a second medical substance that is smaller than that of the first medical substance. The multiple chamber recipient (10, 60) is heated to a predetermined temperature for sterilising the medical substances, and the second chamber (14, 50) with the second medical substance is thermally insulated during heating of the multiple chamber recipient (10, 60). The multiple chamber recipient (10, 60) is held at this temperature for a predetermined time and is subsequently cooled. A predetermined time after commencing heating of the multiple chamber recipient (10, 60) the thermal insulation of the second chamber (14, 50) is removed, so that a defined hold time of the second chamber (14, 50) at the sterilisation temperature is obtained.



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METHOD AND APPARATUS FOR REDUCING THE DEGRADATION OF HEAT SENSITIVE COMPONENTS IN MEDICAL SUBSTANCES DURING HEAT STERILISATION

The present invention concerns a method and an apparatus for reducing the degradation of heat sensitive components in medical substances during heat sterilisation, wherein the medical substances are contained in a multiple chamber recipient that comprises a first chamber with a first medical substance and at least one second chamber with an amount of a second medical substance that is smaller than that of the first medical substance, and the multiple chamber recipient is heated to a predetermined temperature for sterilising the medical substances, is held at this temperature for a predetermined time period and is subsequently cooled.

The method can, for example, be utilised with multiple chamber recipients with medical substances for parenteral feeding/nutrition, however the method is in particular to be used with multiple chamber recipients that contain medical substances for generating a dialysis fluid for peritoneal dialysis.

TECHNICAL BACKGROUND

Currently, haemodialysis is mainly used for acute kidney failure while for chronic kidney failure, besides transplantation, haemodialysis and peritoneal dialysis are utilised. In the case of peritoneal dialysis, the abdominal cavity is repeatedly filled at intervals with a dialysis fluid that is then removed after a hold time. The dialysis fluid is generally a buffered ionic solution with an osmotic means, wherein currently glucose is mainly used as an osmotic means and lactate is mainly used as a buffer. In this way, urea and other substances normally removed from the kidneys and excess water can be removed from the body. These dialysis fluids are produced in factories, transferred to plastic bags of two to five litre capacity and sterilised, in a similar manner to solutions for parenteral nutrition.

A disadvantage of these dialysis fluids is the presence of degradation products. At present, it is assumed that during heat sterilisation these degradation products and the accompanying brownish colour of the fluid are produced by the glucose. It is further presumed that some of these degradation products are responsible for bioincompatability reactions generated by the dialysis fluid. Studies confirm that the degradation products react strongly with biological tissue and have a substantial effect on the immune system and the cells of the peritoneum, either alone or in combination with lactate and/or a low pH value.

Theoretically, the dialysis fluids could be rendered sterile by filtration in place of the heat sterilisation. In practice, however, this is not possible because essentially all countries stipulate that medical solutions must be sterilised by heat.

However, it is known that the degradation of glucose can be markedly reduced when the sterilisation temperature is increased and simultaneously the sterilisation time shortened. It is likewise known that the glucose degradation depends strongly on the pH value, and for example is at its lowest with a pH value between 3.0 and 3.5. However, a peritoneal dialysis fluid with such a low pH value is not permitted for the treatment of patients; for this a pH value of a little over 7 would be optimal, for example 7.1 to 7.4. As a compromise, therefore, a pH value of about 5.3 is set for conventional dialysis fluids. However, from a medical point of view, this is still too low and is probably the cause of infusion pain in some patients. Furthermore substantial amounts of degradation products are still generated during heat sterilisation, which is undesirable for the reasons already mentioned.

An improvement is proposed in WO 93/09820. In the dialysis fluid disclosed here, the glucose is isolated in a small separate second chamber from the rest of the dialysis fluid located in a first chamber. The glucose is separated in this second chamber with a high concentration and a low pH value, so that the formation of degradation products of glucose during heat sterilisation is

substantially reduced. The pH value of the glucose in the separate second chamber is about 3.2, while the remainder of the solution in the larger chamber has a pH value of around 7. After mixing the glucose with the rest of the solution the mixture has a pH value of around 6.4, which offers an additional advantage in terms of tolerance by patients.

In WO 97/05852 a further development of this dialysis fluid is known in which the glucose is separated into two separate chambers, namely a second and third chamber, each with different concentrations. The concentrations are selected such that upon mixing the glucose from the second chamber with the rest of the solution in the first chamber, a dialysis fluid with a glucose concentration of 1.5 % is obtained, upon mixing the glucose from the third chamber with the rest of the solution in the first chamber a glucose concentration of 2.5 % is obtained, and upon mixing the glucose in the second and third chambers with the rest of the solution in the first chamber a glucose concentration of 4 % is obtained. In this way, the three most useful glucose concentrations can be made available with one dialysis fluid recipient, which offers a great advantage in terms of logistics and storage. In addition, this dialysis fluid contains low amounts of degradation products as a result of the low pH values in the second and third chambers.

Although this already represents a clear reduction in the amount of degradation products in the dialysis fluid, there is still a significant amount of degradation products present owing to the high glucose concentration. As a result of the small quantities in the second and third chambers compared to that of the remaining solution in the first chamber, the glucose concentrations in these second and third chambers will be heated much faster during the heat sterilisation than the rest of the solution in the first chamber, which contains the remaining components. This leads to the glucose in the second and third chambers being held for an unnecessary long period at the sterilisation temperature, which results in the unnecessary increase in degradation products. Consequently, while a considerable reduction in degradation products is

achieved compared to conventional dialysis fluids, the quantity of degradation products present is nevertheless still unnecessarily high.

Finally, it is also possible to reduce the formation of degradation products during heat sterilisation of multiple chamber recipients by means of a two step heating procedure. In this, the heating of the multiple chamber recipient in the autoclave is interrupted at a predetermined temperature, so that the temperatures in the first and second, and possibly the third, chamber can become essentially equal. Subsequently, the heating of the multiple chamber recipient proceeds to the predetermined sterilisation temperature. However, it is difficult with this procedure to find the exact intermediate temperature at which no, or only few, degradation products will be formed during the hold period.

DESCRIPTION OF THE INVENTION

In view of this background it is thus an object of the present invention to provide a method, whereby the degradation of heat sensitive components in medical substances during heat sterilisation is reduced, wherein the medical substances are contained in a multiple chamber recipient having a first chamber with a first medical substance and at least a second chamber with an amount of a second medical substance that is smaller relative to the first medical substance, and the multiple chamber recipient is heated to a predetermined temperature to sterilise the medical substances, is held at this temperature for a predetermined time and is subsequently cooled.

This object is achieved in that the second chamber with the second medical substance is thermally insulated during the heating of the multiple chamber recipient.

In this way, a method is provided that reduces the degradation of heat sensitive components in the second chamber during the heat sterilisation of multiple chamber recipients with different substances. The end product after

mixing the contents of the chamber thus likewise contains substantially lower amounts of degradation products.

The second chamber can contain a quantity of a medical substance that is low relative to that in the first chamber. If this substance contains components that form degradation products when held for a long period at the sterilisation temperature, it will be prevented that they are heated faster and consequently remain at the sterilisation temperature longer than the substance in the first chamber. However, it is also possible that the second chamber contains the same amount of a medical substance as the first chamber, but with some of the components of this substance being very heat sensitive, so that they may be subjected to the sterilisation temperature only for a shorter period of time relative to the substance in the first chamber. By means of the thermal insulation of the second chamber, the heating of the second chamber can also be deliberately delayed, as a result of which the desired hold time at the sterilisation temperature can be set.

The hold time of the second chamber at the sterilisation temperature can advantageously be more precisely adjusted, in accordance with a preferred embodiment, when the thermal insulation is removed at a predetermined time after commencing the heating of the multiple chamber recipient. In this way the point in time at which the second chamber of the multiple chamber recipient is also exposed to the heating environment can be accurately set. Furthermore, since the point in time of the cooling of the multiple chamber recipient is also predetermined, a precisely controlled heat sterilisation with a defined hold time at the sterilisation temperature is also separately possible for the second chamber.

In accordance with a further preferred embodiment, the time for removing the thermal insulation is advantageously determined such that the first and second medical substances in the first and second chambers have essentially the same F value at the end of the hold time. F is utilised here as a gauge of the capacity of a sterilisation process to kill microbes, or the

sterilisation capacity of a sterilisation process, and is predominantly utilised in the food industry and in medicine. It is a reference gauge and signifies a specific rate of microbes killed during a sterilisation process, F representing the time required to achieve this specific death rate at 121 °C.

If the first and second medical substances have essentially the same F value, then this indicates that both substances have undergone essentially the same degree of sterilisation and, in particular, that the second chamber or the second substance has not been subjected to an unnecessary over-sterilisation as a result of overheating. Overheating the second chamber would lead to a substantial increase in the degradation products. It is to be noted at this point that a correlation exists between the F value and the degradation in the sense that with an increasing F value, the degradation products also increase, and vice versa.

In order to achieve an adequate sterilisation of the multiple chamber recipient, the latter is advantageously heated to a temperature of between 100°C and 135°C, preferably to a temperature of 121 °C. The sterilisation process is advantageously controlled such that the multiple chamber recipient is held for between 1 minute to several hours at this predetermined temperature, and preferably 15 minutes.

The method for reducing the degradation of heat sensitive components in medical substances described here is not limited only to multiple chamber recipients with two chambers, but may also be applied to multiple chamber recipients with more than two chambers. Therefore, according to another preferred embodiment, the method is utilised for a multiple chamber recipient that additionally includes a third chamber with an amount of a third medical substance that is smaller relative to that of the first medical substance, the third chamber being thermally insulated together with the second chamber during heating of the multiple chamber recipient. Here also the second chamber with the second medical substance and the third chamber with the third medical substance are advantageously arranged in a thermally insulating jacket, that is

opened a predetermined time after commencing heating of the multiple chamber recipient. The second chamber and the third chamber can contain different amounts of the same substance or also the same amount of different substances.

The time at which the thermal insulation is removed is likewise advantageously defined such that the first and second and third medical substances in the first and second and third chambers have essentially the same F value at the end of the hold time. If the second and third chambers contain different amounts of a medical substance, the F value of the largest amount is determinate for the removal of the thermal insulation. This should be essentially the same as the F value in the first chamber. The F value of the smaller amount in the other chamber will then be somewhat higher; this deviation from the desired F value has to be accepted in view of the required sterilisation of the larger amount. However, in order to achieve a nearly equivalent F value in this case also, the insulation can be formed differently in areas. For example, it could be formed thinner in the area of the second or third chamber, when these contain a larger amount, so that the sterilising heat reaches the large amount before the removal of the insulation and is able to heat this a little. Or, the second and third chambers will be respectively insulated such that the insulation of each can be successively removed independently of one another.

The thermally insulating jacket may take any desired form. For example, it can consist of an insulating material which, upon reaching a predetermined temperature will collapse or shrink, thus allowing the elevated surrounding temperature to reach the multiple chamber recipient. In this way the heating of the second and possibly also the third chamber will be delayed, and as a result, the time during which the second and possibly the third chamber are held at the sterilisation temperature can be controlled.

Another possibility for a thermally insulating jacket is a container with thermally insulating walls. The second and possibly the third chamber would be laid in this container with the first chamber remaining outside, and the container would be closed. In this manner, the second and possibly the third chamber will be thermally insulated, so that initially only the first chamber is heated. When the predetermined point in time is reached, the container is opened and the second chamber and possibly third chamber will be exposed to the sterilising heat and heated to the same temperature as the first chamber. In this way, the hold time of the second and possibly third chambers can be precisely determined independently of that of the first chamber. When the predetermined hold time of the first chamber is terminated, the multiple chamber recipient is cooled down. During this, care should be taken that the cooling occurs rapidly, so that degradation products are not formed unnecessarily as a result of slow cooling.

The method can be applied to multiple chamber recipients of any desired form, however it is advantageously utilised with a multiple chamber recipient formed as a flexible bag. The method can likewise be applied to multiple chamber recipients that hold any desired medical substance. For example, the multiple chamber recipient may hold substances for parenteral feeding. Also, the substances can take any desired form. For example, the medical substances can be solutions in liquid form, they can also be concentrates in powder form. However, the method is preferably applied to multiple chamber bags containing medical substances for the production of a dialysis fluid for peritoneal dialysis. According to a preferred embodiment, the second medical substance and third medical substance in the second and third chambers, respectively, comprise different concentrations of glucose, that is required for the dialysis fluid, or, according to another preferred embodiment, the same concentration of glucose in different quantities.

DESCRIPTION OF THE DRAWINGS

Examples for the method according to the invention are given by way of illustration in the accompanying drawings. The figures contained therein show the temperature curve and the F curve and thus the degradation, on the one hand, for the sterilisation of a double chamber bag according to conventional heat sterilisation in an autoclave, and on the other hand, for the heat sterilisation of a double chamber bag in an autoclave with the method according to the invention. Therein, the F value "F_o" is the F value corresponding to a sterilisation temperature of 121 °C. There is shown in

Fig. 1 the temperature curve in °C over time in minutes during the conventional heat sterilisation of a double chamber bag;

Fig. 2 the F_o value over time in minutes during the heat sterilisation according to Fig. 1;

Fig. 3 the temperature curve in °C over time in minutes during the heat sterilisation of a double chamber bag according to the method of the invention;

Fig. 4 the F_o value over the time in minutes during the heat sterilisation of Fig. 3;

Fig. 5 a double chamber bag;

Fig. 6 a triple chamber bag;

Fig. 7 an apparatus for carrying out the method according to the invention; and

Fig. 8 the apparatus of Fig. 7 in a closed state.

DESCRIPTION OF PREFERRED EMBODIMENTS

In Fig. 1 there is shown the temperature curve of a double chamber bag during a conventional heat sterilisation in an autoclave, wherein the dashed line 1 shows the temperature curve in the second chamber, and the continuous line 3 shows the temperature curve in the first chamber. The second chamber contains a smaller quantity of medical substance compared to the first chamber.

Therefore, the contents of the second chamber will be heated faster during heating of the multiple chamber bag, as can be clearly seen from the temperature curve (line 1) in the second chamber during the first ten minutes. The second chamber reaches the sterilisation temperature, which here is about 121 °C, much faster, and is also held there substantially longer than the first chamber. The first chamber needs a longer period for heating owing to the larger quantity of medical substance, as is evident from the temperature curve (line 3) during the first ten minutes. The first chamber reaches the sterilisation temperature much later and is also held at this sterilisation temperature for a shorter period (line 3). After reaching the end of the predetermined hold time at the sterilisation temperature for the multiple chamber recipient or for the first chamber, the multiple chamber recipient is cooled down. During this, the second chamber, or the contents of the second chamber, cools faster (line 1) owing to the smaller quantity of medical substance relative to that of the first chamber (line 3). The longer hold time of the second chamber at the sterilisation temperature causes a higher formation of degradation products and also leads to an elevated F value in the second chamber, which is superfluous in terms of sterilisation.

This is shown in Fig. 2. Fig. 2 shows the F_o curve during the heat sterilisation according to Fig. 1. As can be clearly seen here, in the second chamber (line 1) an F_0 value is obtained that is almost double that in chamber 1 (line 3). The F_o value of about ten obtained in chamber 1 is a normally sought and sufficient F_o value for sterilisation, while the F_o value obtained in the second chamber of around twenty is unnecessarily high.

To avoid this over-sterilisation and the accompanying increased degradation of, for example, glucose contained in the second chamber, the second chamber is provided with a thermally insulating jacket, that is removed a predetermined time after the beginning of the heating process. The resulting temperature curve during heat sterilisation is shown in Fig. 3. Here it can be seen clearly that the beginning of the heating of the second chamber (line 2) is

markedly delayed compared to the beginning of the heating of the first chamber (line 3). After about twenty minutes, the thermally insulating jacket of the second chamber is removed, so that the second chamber is likewise heated rapidly to the sterilisation temperature, together with the first chamber. After a predetermined hold time of the multiple chamber recipient at the sterilisation temperature, the multiple chamber recipient is cooled, as is apparent from the continuing temperature curve of the first and second chambers (line 3, line 1).

In contrast to the heat sterilisation of the multiple chamber recipient without the thermal insulation of the second chamber according to Fig. 1, the second chamber here remains held at the sterilisation temperature essentially as long as the first chamber. In this way, on the one hand, the excessive and unnecessary formation of degradation products is prevented and, on the other, an over-sterilisation of the medical substance contained in the second chamber is avoided.

This is shown in Fig. 4. Fig. 4 shows the F_o curve during the heat sterilisation according to Fig. 3. Because the first and second chambers, or their contents, are held for essentially the same time at the sterilisation temperature, the result is an almost identical F_o value. The F_o value of the medical substance in the second chamber (line 1) differs only slightly from the F_o value of the substance in the first chamber (line 3). Due to the later commencement of heating and the slightly higher temperature relative to that of the first chamber during the hold time, the F_o temperature curve of the second chamber (line 1) lies slightly below the F_o temperature curve of the first chamber (line 3) at the beginning, but then lies slightly above it at the end of the sterilisation. However an over-sterilisation of the second chamber has not occurred, nor were excessive degradation products formed in the second chamber during the sterilisation.

The method performed here by way of example on a two chamber bag can also be applied to three or multiple chamber bags, as described in detail above. In this case, the larger first chamber, or the first chamber filled with the

larger amount of medical substance, determines the hold time of the multiple chamber bag in the autoclave, while the chamber of the second, and possibly third, fourth, etc. chambers provided with a thermally insulating jacket that includes the largest amount of medical substance, determines the time of removal of the thermally insulating jacket. The desired, lowest required F value, that corresponds to an adequate sterilisation, is always to be selected as a gauge for the hold time of the multiple chamber recipient in the autoclave or for the removal of the thermal insulation.

In Fig. 5 a double chamber bag 10 is shown, that is to be sterilised according to the method of the invention. The multiple chamber bag 10 includes a first larger chamber 12 and a second smaller chamber 14. In the present case, the multiple chamber recipient 10 contains a dialysis solution for peritoneal dialysis and includes an electrolytic solution in the first chamber 12 and a glucose solution in the second chamber 14.

The first chamber 12 is separated from the second chamber 14 by a welded seam 16, in which there is arranged a connecting tube 26. The connecting tube 26 is closed at one end by a break-off seal 28. A fill tube 20, through which the second chamber 14 is filled, is connected at the upper edge 18 of the multiple chamber recipient 10. The outer end of the fill tube 20 is provided with a seal 22 which may be achieved simply by melting the end of the fill tube 20 for example. Moreover, at the upper edge 18 there is provided an opening 24, by which the multiple recipient bag 10 can be suspended. At the lower edge 30 of the multiple chamber recipient 10, there is arranged a connection tube 32, by means of which the contents of the first chamber 12 can be supplied to a patient, who is not shown. Furthermore, there is also provided a fill tube 20 at the lower edge 30, through which the first chamber 12 is filled. This fill tube 20 is also provided with a seal 22 at its outer end. Finally, a feed tube 34 is also arranged at the lower edge 30, by means of which medication can be supplied to the contents of the first chamber 12, for example. The feed tube 34 is closed at its outer end with a septum 36, so that the injection of

medication into the first chamber 12 is possible. Before the dialysis solution is administered to the patient, the contents of the first chamber 12 and second chamber 14 are mixed together. To this end, the break-off seal 28 is broken off so that the connecting tube 26 between the first chamber 12 and the second chamber 14 is opened. The contents of the second chamber 14 then run through the connecting tube 26 into the first chamber 12, and mix with the solution located therein. Subsequently, the mixed solution can be supplied to the patient through the connecting tube 32.

It is again to be noted at this point that the multiple chamber recipient 10 can also include a third, or even more chambers, the contents of which would also be mixed with the contents of the first chamber 12 to obtain the desired solution. As an example of this, a triple chamber bag 60 is shown in Fig. 6. This includes a third chamber 50 that is separated from the second chamber 14 by a welded seam 52. By means of a fill tube 20, that is likewise provided here, the third chamber 50 can be filled, and by means of a connecting tube 26, its contents can be fed into the first chamber 12 for mixing with the contents of the first chamber. Otherwise, like parts are denoted by like reference numerals so that a further description can be dispensed with.

In Fig. 7 there is shown an apparatus 40 for insulating the second chamber of the multiple chamber recipient 10 during the heat sterilisation. The apparatus includes an upper portion 42 and a lower portion 44 that are connected together by a joint 46. The upper portion 42 and the lower portion 44 are each box-shaped and comprise thermal insulation 48 on their inner sides.

The multiple chamber recipient 10, that has already been described extensively with reference to Fig. 5, is laid with its first chamber 14 in the lower portion 44 of the apparatus 40. Care should be taken when doing this that the multiple chamber recipient 10 lies with the welded seam 16 on the edge of the lower portion 44. If the multiple chamber recipient 10 were to comprise several chambers requiring thermal insulation during the heat sterilisation of the

multiple chamber recipient 10, these would also be arranged in the lower portion 44 of the apparatus 40.

When the apparatus 40 is closed by lowering the upper portion 42 down on the lower portion 44, the second chamber 14 of the multiple chamber recipient 10 is thermally insulated. This is shown in Fig. 8.

If the multiple chamber recipient 10 shown here is heat sterilised, for example in an autoclave, with its second chamber 14 thermally insulated by means of the apparatus 40, initially only the first chamber 12 will be heated. After the elapse of a predetermined time, the apparatus 40 will be opened by raising the upper portion 42, which can be achieved by appropriate means known to the person skilled in the art (this open condition corresponds approximately to that of the open apparatus 40 shown in Fig. 7). Hence the second chamber 14 of the multiple chamber recipient 10 will also be exposed to the sterilisation temperature and heated. In this way the hold time of the second chamber 14 at the sterilisation temperature can be intentionally controlled, as described in detail above.

List of reference numerals

10	bag
12	first chamber
14	second chamber
16	welded seam
18	upper edge
20	fill tube
22	seal
24	opening
26	connecting tube
28	break-off seal
30	lower edge
32	connecting tube
34	feed tube
36	septum
40	apparatus
42	upper portion
44	lower portion
46	joint
48	thermal insulation
50	third chamber
52	welded seam
60	triple chamber bag

CLAIMS

1. Method for reducing the degradation of heat sensitive components in medical substances during heat sterilisation, wherein the medical substances are contained in a multiple chamber recipient (10) that comprises a first chamber (12) with a first medical substance and at least one second chamber (14) containing an amount of a second medical substance that is smaller than that of the first medical substance,
and the multiple chamber recipient (10) is heated to a predetermined temperature for sterilising the medical substances, is held at this temperature for a predetermined time period and is subsequently cooled,
characterized in that the second chamber (14) with the second medical substance is thermally insulated during the heating of the multiple chamber recipient (10).

2. Method as claimed in claim 1, **characterized in that** the thermal insulation is removed a predetermined time after commencing heating of the multiple chamber recipient (10).

3. Method as claimed in claim 2, **characterized in that** the time for removing the thermal insulation is determined such that at the end of the hold time the first and second medical substances have essentially the same F-value.

4. Method as claimed in any previous claim, **characterized in that** the multiple chamber recipient (10) is heated to a temperature between 100 °C and 135 °C.

5. Method as claimed in claim 4, **characterized in that** the multiple chamber recipient (10) is heated to a temperature of 121 °C.

6. Method as claimed in any one of the previous claims, **characterized in that** the multiple chamber recipient (10) remains between 1 minute and several hours at the predetermined temperature.

7. Method as claimed in claim 6, **characterized in that** the multiple chamber recipient (10) remains at the predetermined temperature for 15 minutes.

8. Method as claimed in any one of the previous claims, **characterized in that** the multiple chamber recipient (10) contains a third chamber with an amount of a third medical substance that is smaller than that of the first medical substance, the third chamber being thermally insulated together with the second chamber (14) during heating of the multiple chamber recipient (10).

9. Method as claimed in claim 8, **characterized in that** the second chamber (14) with the second medical substance and the third chamber with the third medical substance are arranged in a thermally insulating jacket (40), that is removed a predetermined time after commencing heating of the multiple chamber recipient (10).

10. Method as claimed in claim 9, **characterized in that** the time for removing the thermally insulating jacket (40) is determined such that the first substance and second and/or third medical substance have essentially the same F value at the end of the hold time.

11. Method as claimed in any preceding claim, **characterized in that** the multiple chamber recipient is a flexible bag (10).

12. Method as claimed in claim 11, **characterized in that** the multiple chamber recipient (10) contains medical substances for producing a dialysis fluid for peritoneal dialysis.

13. Method as claimed in claim 12, **characterized in that** the second medical substance and the third medical substance contain the glucose required for the dialysis fluid in different concentrations, respectively.

14. Method as claimed in claim 12, **characterized in that** the second medical substance and the third medical substance contain the glucose required for the dialysis fluid in the same concentrations in different amounts, respectively.

15. Method as claimed in claim 11, **characterized in that** the multiple chamber recipient (10) contains medical substances for parenteral feeding.

16. Method as claimed in any preceding claim, **characterized in that** the heating of the multiple chamber recipient (10) is interrupted at least once at a predetermined temperature for a predetermined time.

17. Apparatus for reducing the degradation of heat sensitive components in medical substances during heat sterilisation, wherein the medical substances are contained in a multiple chamber recipient (10) that comprises a first chamber (12) with a first medical substance and at least one second chamber (14) containing an amount of a second medical substance that is smaller than that of the first medical substance,
and the multiple chamber recipient is heated to a predetermined temperature for sterilising the medical substances, is held at this temperature for a predetermined time period and is subsequently cooled,
characterized in that the apparatus (40) comprises a movably arranged thermal insulation (48), such that, on the one hand, the second chamber (14) of the multiple chamber recipient (10) is essentially completely surroundable by the thermal insulation (48), and on the other hand, the thermal insulation (48) is at least partially removable from the second chamber (14) of the multiple chamber recipient (10).

18. Apparatus as claimed in claim 17, **characterized in that** the apparatus comprises a closable container (40) with an upper portion (42) and a lower portion (44) that are connected with one another by a joint (46), and each have thermal insulation (48).

19. Apparatus as claimed in claim 18, **characterized in that** a thermally insulated cavity for receiving the second chamber (14) of the multiple chamber recipient (10) is formed between the upper portion (42) and the lower portion (44).

Fig.1

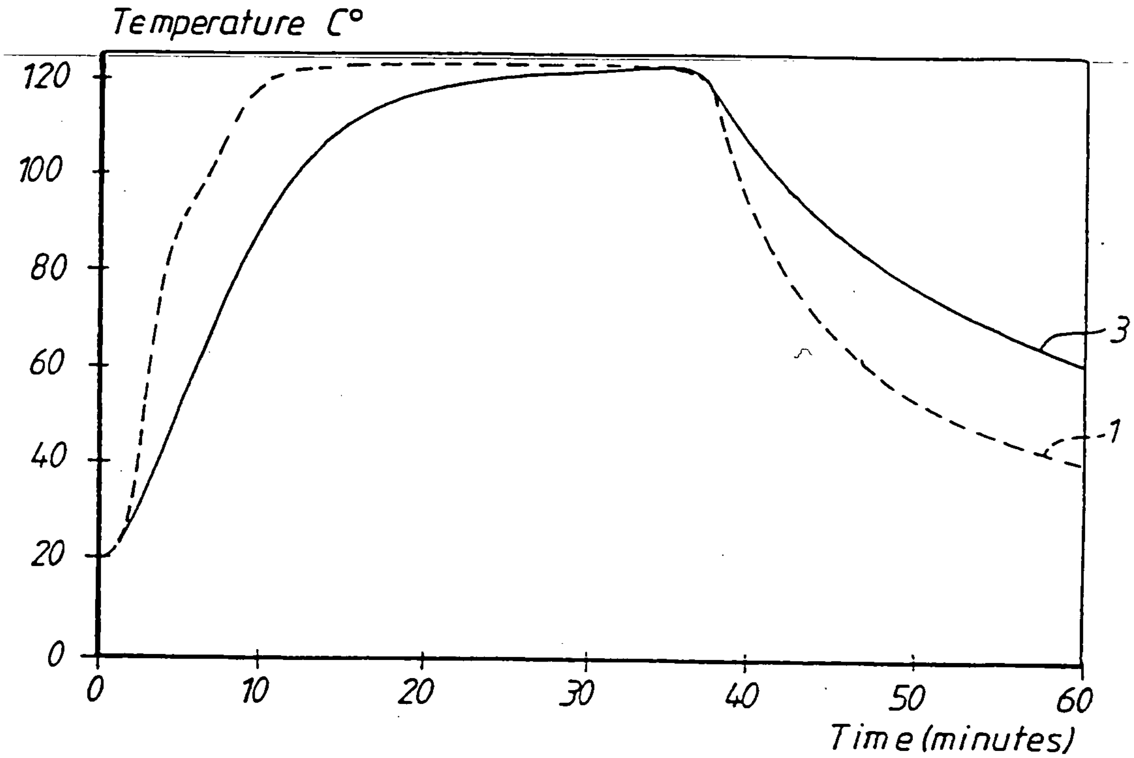

Temperature C°
120
100
80
60
40
20
0
0
10
20
30
40
50
60
Time (minutes)
3
1

Fig.2

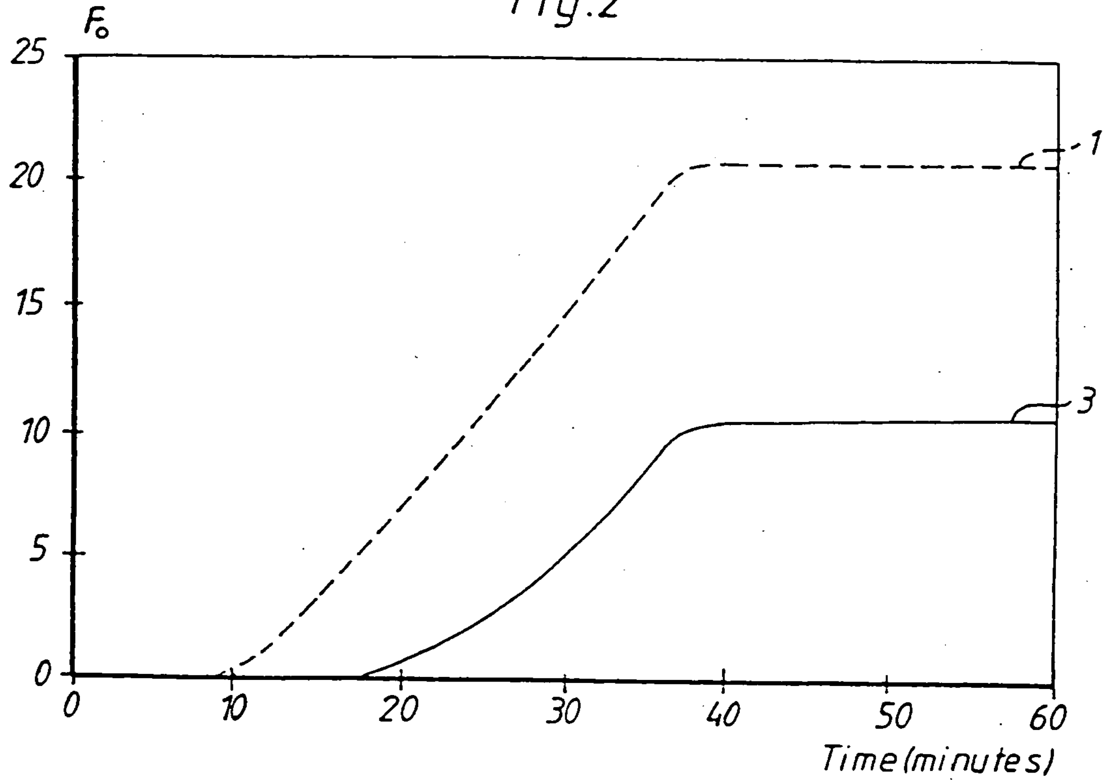
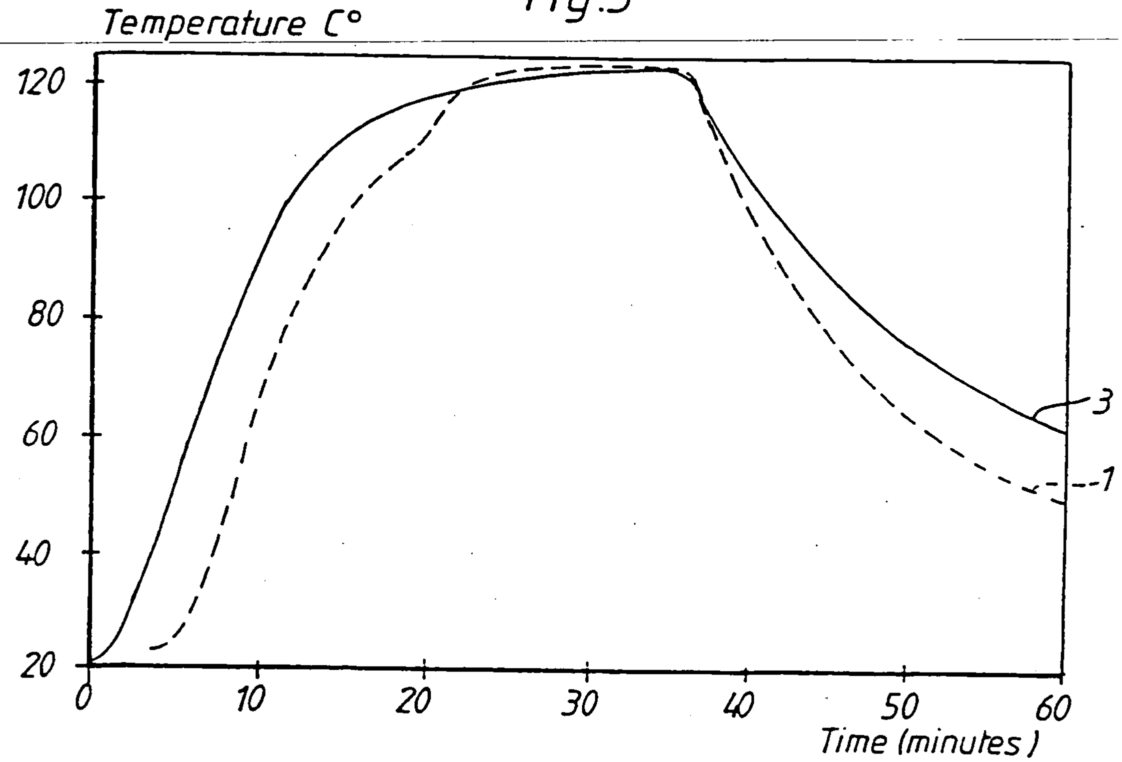

F_0
25
20
15
10
5
0
0
10
20
30
40
50
60
Time (minutes)
1
3

Fig.3


Temperature C°
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100
80
60
40
20
0
10
20
30
40
50
60
Time (minutes)
3
1

Fig.4

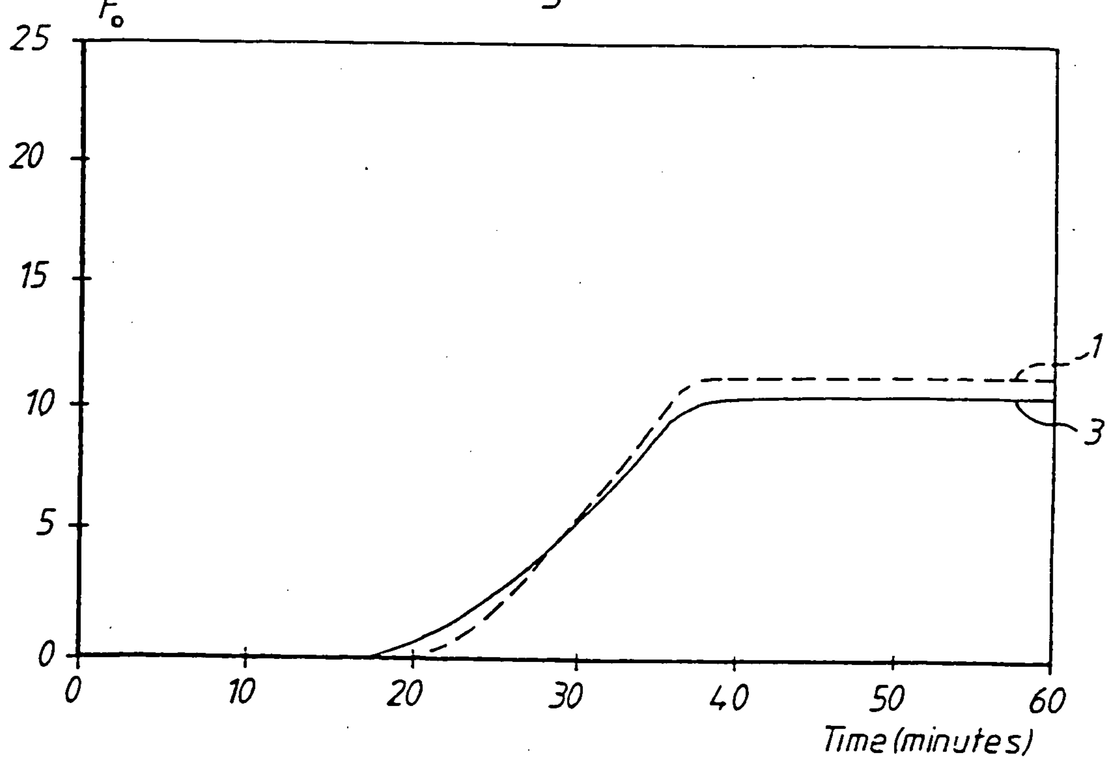

F_o
25
20
15
10
5
0
0
10
20
30
40
50
60
Time (minutes)
1
3

Fig.5

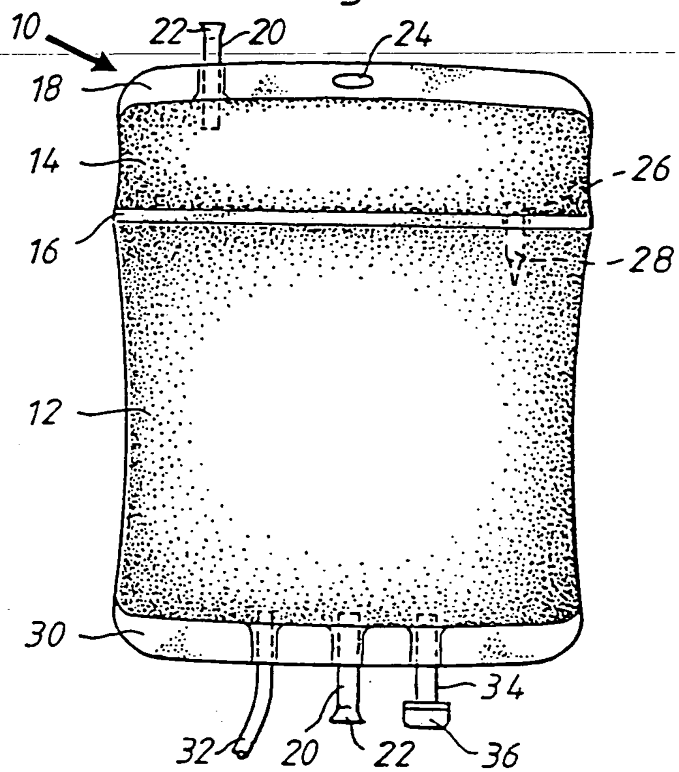
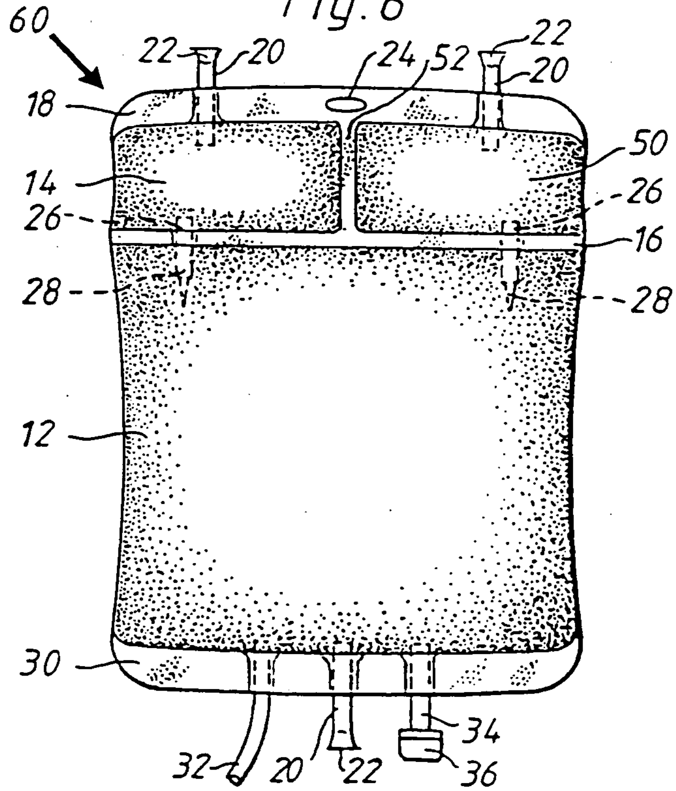

10
22
20
24
18
14
26
16
28
12
30
34
32
20
22
36

Fig.6


60
22
20
24
52
22
20
18
50
14
26
26
16
28
28
12
30
34
32
20
22
36

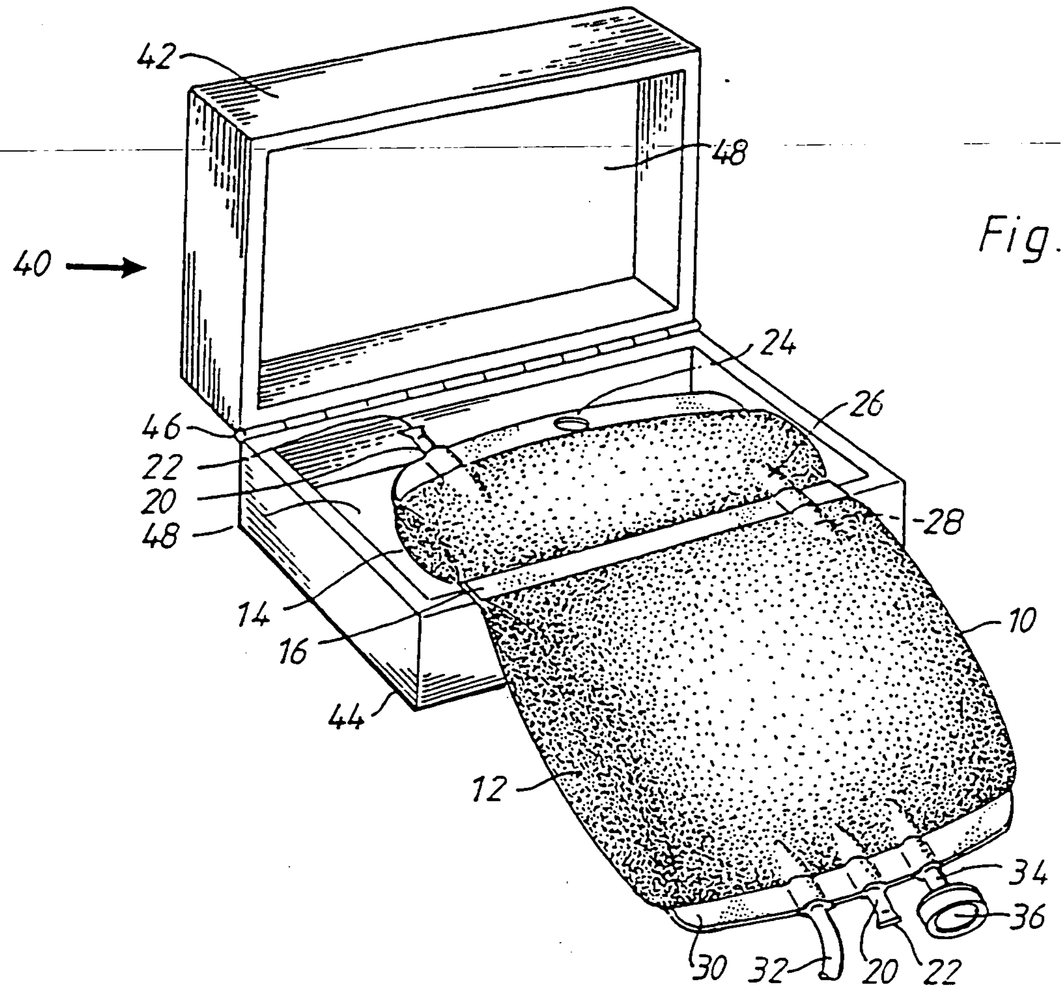

42
48
40
24
26
46
22
20
48
28
14
16
10
44
12
34
36
30
32
20
22

Fig.7

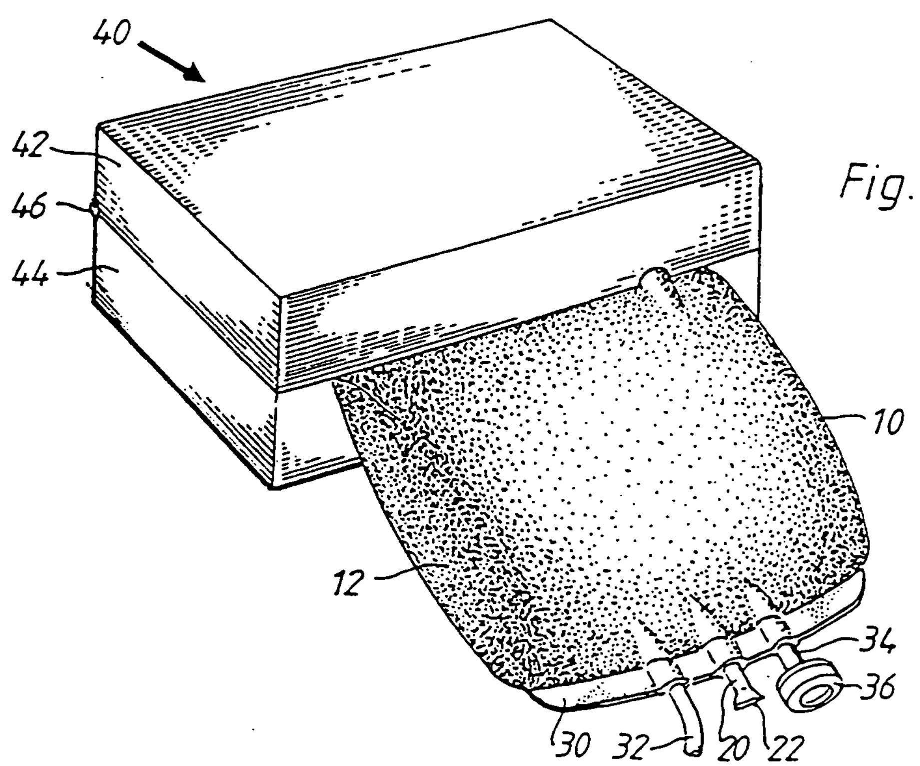

40
42
46
44
10
12
34
36
30
32
20
22

Fig.8

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 99/01889

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: A61L 2/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPI, EPODOC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DE 4321999 C1 (FÜRSTLICH HOHENZOLLERNSCHE WERKE LAUCHERTAHL GMBH & CO), 13 October 1994 (13.10.94), figure 1, claims 1-17 --	1-19
A	WO 9309820 A1 (GAMBRO AB), 27 May 1993 (27.05.93), figure 1, claims 1-13 --	1-19
A	WO 9705852 A1 (GAMBRO AB), 20 February 1997 (20.02.97), figure 1, claims 1-11 -- --------	1-19

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

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"A" document defining the general state of the art which is not considered to be of particular relevance

"E" erlier document but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 January 2000	17 -02- 2000
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer Agneta Änggård/mj Telephone No. +46 8 782 25 00

INTERNATIONAL SEARCH REPORT

Information on patent family members

02/12/99

International application No.
PCT/SE 99/01889

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 4321999 C1	13/10/94	NONE	
WO 9309820 A1	27/05/93	EP 0668785 A	30/08/95
		EP 0951915 A	27/10/99
		JP 7500992 T	02/02/95
		SE 9103395 D	00/00/00
		US 5536469 A	16/07/96
WO 9705852 A1	20/02/97	EP 0845970 A	10/06/98
		JP 11510414 T	14/09/99
		SE 510030 C	12/04/99
		SE 9502769 A	09/02/97